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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,507	11/05/2003	Ali Amara	03495.0301	6288

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 06/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/700,507	AMARA ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24,25,27-29,31-34,36,40,81-84,91,92,94-96,98-105,110 and 111* is/are pending in the application.

4a) Of the above claim(s) *81-84,104 and 105* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24,25,27-29,31-34,40,91,92,94-96,98-103,110 and 111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response filed April 13, 2006 is acknowledged and entered. Claims 24, 25, 27-29, 31-34, 36, 40, 81-84, 91, 92,94-96, 98-105, 110 and 111 are pending. Claims 81-84, 104 and 105 are withdrawn from consideration, being drawn to non-elected subject matter. Claims 24, 25, 27-29, 31-34, 36, 40, 91, 92, 94-96, 98-103, 110 and 111 are under examination. This Office action is non-final in view of the new grounds of rejection set forth below. Any inconvenience is regretted.

Response to Amendment

The rejection of claims 36, 102, 110 and 111 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement with respect to the availability of monoclonal antibody Mab 1B10.2.6 from hybridoma cell 1B10.2.6, is withdrawn in view of Applicant's submission of the deposit declaration filed April 13, 2006.

The provisional rejection of claims 2, 10-12, 87, 88, 113 and 114 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 23-34, 78-89 and 96-100 of copending Application No. 10/700,491, is moot in view of the cancellation of claims 2, 10-12, 87, 88, 113 and 114.

The rejection of claims 2, 10, 87, 88, 113 and 114 under 35 U.S.C. 102(a) as being anticipated by Littman *et al.* (WO 01/64752 A2, "Littman") is moot in view of the cancellation of claims 2, 10, 87, 88, 113 and 114.

The rejection of claims 2, 10, 87, 88, 113 and 114 under 35 U.S.C. 102(b) as being anticipated by Figdor *et al.* (EP 1046651 A1, "Figdor") is moot in view of the cancellation of claims 2, 10, 87, 88, 113 and 114.

The rejection of claims 2, 10-12, 24-34, 36, 40, 87-103, 110-115 under 35 U.S.C. 102(b) as being anticipated by Gehrz *et al.* (WO 91/05876, herein, "Gehrz"), is moot in view of the cancelled claims, and withdrawn in view of Applicant's amendment and persuasive arguments. Applicant points out the claims require the molecule to bind the DC-SIGN receptor. Gehrz's method treats CMV with monoclonal antibodies, one of which binds to gp55, a subunit of envelope glycoprotein B (abstract and Example 1). The DC-SIGN receptor is not gp55, thus Gehrz's teachings do not anticipate the claimed invention.

Claim Rejections - 35 USC § 112

(*New Rejection*) Claims 24, 25, 27-29, 31-34, 36, 40, 91, 92, 94-96, 98-103, 110 and 111 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to a method of treating a cytomegalovirus virus (CMV) infection or HIV infection of a mammal comprising, administering to the mammal a molecule that binds to the DC-SIGN receptor. The identity of the DC-SIGN receptor is not clear. According to the specification,

- DC-SIGN is the ligand of ICAM-3, which enables transient DC-T cell interactions, thus facilitating primary immune response [008]. DC-SIGN is expressed on dendritic

cells and ICAM-3 is expressed on T-cells. According to this definition, the claimed method involves administering a molecule that binds ICAM-3.

- DC-SIGN and DC-SIGN receptor are synonymous terms [051]. The acronym, "DC-SIGN" does not include the term "receptor". It is unclear how a ligand (DC-SIGN) and its receptor (DC-SIGN receptor) can be one and the same. Clarification is required.

Based on these two definitions, the metes and bounds of the term, "DC-SIGN receptor" cannot be determined. The methods of treating also take on a different meaning when viewed in light of these two definitions. Either the method involves administering a molecule that binds to ICAM-3, or the molecule binds to the DC-SIGN (or DC-SIGN receptor?) on the dendritic cell, thus blocking virus binding and entry.

Claims Summary and Interpretation

The claims are drawn to a method of treating a CMV infection of a mammal or inhibiting entry of a CMV virus into a cell of a mammal, comprising administering to the mammal a molecule that specifically binds to a DC-SIGN receptor. The molecule is administered in an amount sufficient to inhibit the binding of the CMV virus to the DC-SIGN receptor. Specifically, the molecule that binds to the DC-SIGN receptor is a CMV envelope glycoprotein B, or a binding moiety thereof. In another embodiment, the molecule that binds to the DC-SIGN receptor is an antibody, Mab1B10.2.6.

In another embodiment, the claims are drawn to a method of treating an HIV infection or inhibiting entry of an HIV virus into a cell of a human, comprising administering a binding

moiety of the CMV envelope glycoprotein B that binds to the DC-SIGN receptor, thus inhibiting the binding of HIV gp120 to the DC-SIGN receptor.

Claim Rejections - 35 USC § 112

Claims 24, 25, 27, 29, 31-34, 40, 91, 92, 94, 96, 98-101 and 103 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims encompass the treatment of CMV and HIV infection, wherein a competitive inhibitor (effector molecule) inhibits binding of a pathogen to a DC-SIGN receptor. Clearly, Applicant has not demonstrated possession of a method that treats CMV or HIV wherein the molecule that binds DC-SIGN is any molecule other than those disclosed, such as mannan, Mab1B10.2.6 and glycoprotein B. Claiming "a binding moiety" of CMV envelope glycoprotein B that binds DC-SIGN receptor is not adequately provided for in the specification. Claiming any antibody that binds DC-SIGN receptor is also not provided for. The specification does not put one of skill in possession of the large genus of methods claimed.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

In this case, the only factor present in the claim is a structure (binding moiety of glycoprotein B, or a generic antibody, or generic molecule) and a function of competitively inhibiting binding of a virus to DC-SIGN. Given the structure of glycoprotein B, one of skill in the art needs to be provided with some core structure of the glycoprotein that needs to be retained in order to arrive at binding moiety that functions as claimed. Given the structure of an antibody, one of skill in the art must be given the structure to which it must bind. Given the generic molecule that binds DC-SIGN receptor, one of skill must be provided with some structure to begin with. And, in all these instances, the resulting binding molecule must be able to compete with virus binding DC-SIGN receptor *in vivo* to the degree that a patient is treated.

Since Applicant has not provided this information (structure, and structure/function correlation), the full scope of the claims is not adequately described. Applicant is not entitled to claim a method of treating CMV or HIV with the large genus of molecules encompassed by the claims. Three examples (mannan, Mab1B10.2.6, and glycoprotein B) are not representative of the genus represented by the term, "molecule". Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus of methods.

(*New Rejection*) Claims 24, 25, 27-29, 31-34, 36, 40, 91, 92, 94-96, 98-103, 110 and 111 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to a method of

treating a CMV or HIV virus infection *in vivo* comprising, administering to the mammal a molecule that binds to the DC-SIGN receptor. The identity of the DC-SIGN receptor is not clear (see above).

If the method of treatment encompasses administering to a mammal a molecule that binds to the mammal's ICAM-3 (a DC-SIGN receptor), then the specification is completely non-enabled. Applicant has failed to explain how binding ICAM-3 would inhibit binding between DC-SIGN and CMV or HIV, for example.

If the method of treatment encompasses administering to a mammal a molecule that binds to the mammal's DC-SIGN expressed on their dendritic cells, then the method claims are non-enabled for their asserted ability to treat a CMV or HIV virus infection *in vivo*. The Office recognizes that methods of treatment were previously indicated as enabled by the specification. However, upon further consideration of the state of the art and Applicant's disclosure, methods of treatment are not adequately enabled by the specification such that one of skill in the art would be equipped to practice the claimed methods.

The breadth of the claims is unreasonable, encompassing the inhibition of binding between the CMV and HIV virus and the mammal's dendritic cells, in a mammal already infected with the virus.

The nature of the invention is the inhibition of CMV or HIV by blocking entry of these viruses into dendritic cells by preventing a viral molecule (such as envelope) from binding DC-SIGN.

The state of the art surrounding DC-SIGN and CMV infection is that experiments have demonstrated a relationship between DC-SIGN and CMV glycoprotein B. Also known is that

DC-SIGN was shown to bind HIV particles through a carbohydrate recognition domain of DC-SIGN and sugar moieties of HIV-1 gp120 (page 63, paragraph [0148]).

The level of skill in the art is high, evidenced by those of skill in the prior art and the instant inventors.

The level of predictability in the art is low because the mechanism described in this invention is novel, and thus *in vivo* experimentation is required to determine whether *in vitro* results reflect *in vivo* performance. Competitive binding of dendritic cells is a complex mechanism. Extrapolating a competitive binding assay in vitro to an in vivo human treatment is not substantiated because the concept of using DC-SIGN receptor competitive binding for these two viruses is novel. One cannot predict the outcome a new mechanism that has only been demonstrated in vitro. Treatment of HIV and CMV would indicate that there is a therapeutic benefit to administering a DC-SIGN receptor to a patient infected with HIV or CMV. Applicant has not demonstrated treatment of any sort.

The specification does not provide guidance for inhibiting virus entry *in vivo*. If one of skill in the art were to treat a CMV or HIV infection, given the claimed methods and specification, one would not know what dosage of antibody, for example, should be used for binding DC-SIGN. Given the abundance of dendritic cells in an individual, one would have to consider what dosage of antibody would be appropriate for binding a significant number of dendritic cells such that the virus (already present in the body) would be inhibited. Applicant has not taught what effective amount of antibodies would result in a therapeutic benefit for the patient (an improvement in a symptom).

The working examples include *in vitro* binding inhibition of CMV and HIV (indirectly through CMV). While this data is useful for demonstrating that there is relationship between DC-SIGN and said viruses, the data cannot be extrapolated to methods of improving the symptoms of any and all mammals infected with these pathogens.

Given the breadth of the claims, the nature of the invention, the state of the prior art, the level of skill in the art, the low level of predictability, the lack of guidance and working examples, it would require undue experimentation to use the claimed invention as claimed. Further experimentation is required before *in vivo* applications are adequately enabled. Given this new mechanism of virus inhibition, one of skill cannot predict the *in vivo* results with any degree of certainty. Therefore, the claims are not enabled by the specification.

Conclusion

No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Stacy B Chen 6/22/06

Stacy B. Chen
Primary Examiner
June 22, 2006